REMARKS

Claims 1, 4-7 and 23 are pending in the application. In the present amendment claims 1 and 23 have been amended to recite that the trkC receptor to which the antibody binds is a full-length trkC receptor comprising amino acid residues 32 to 839 SEQ ID NO: 6 and that binding of a such an antibody inhibits the activity of the trkC receptor. Support for this amendment is found in the specification and claims as originally filed, for example, at page 5, lines 12-15; page 6, lines 15-16; page 12, lines 21-27; page 13, lines 10-11 and 16-17; page 68, lines 28-29, and original claims 14 and 18.

No new matter is introduced by way of the claim amendment.

Priority

The full-length trkC sequence of SEQ ID NO: 6 is found in the priority application Serial No. 08/215,139 filed on March 18, 1994. The use of trkC antibodies for the treatment of axonal sprouting in epilepsy is also mentioned (*e.g.*, page 88, lines 6-7). Accordingly, applicants submit that the priority date of the present application is March 18, 1994.

Rejections

Claims 1, 4-7, and 23 stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. Claims 1, 4-7, and 23 stand rejected for alleged lack of written description. These rejections are respectfully traversed.

The Rejections of Claims 1, 4-7, and 23 Under 35 U.S.C. §112, First Paragraph for Alleged Lack of Enablement

Claims 1, 4-7, and 23 stand rejected as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

In support of the rejection, the Examiner acknowledges that "the association between neuronal sprouting and epilepsy was well known in the art at the time the invention was made" (page 4, lines 6-8, Office action dated 3/28/2005) but suggests that "nothing in any of these references suggests an association between that sprouting and 'a' TrkC as suggested by Applicant" (page 4, lines 8-9, Office action dated 3/28/2005).

As indicated in this Office Action by the quotation marks around the word "a" in the phrase "'a' TrkC," and as indicated by the more extensive discussion in a previous Office Action (e.g., page 3, lines 4-18, Office action dated 07/23/2004) the Examiner is concerned that "not only the full-length receptor but also its truncated and variant forms such as those arising by alternate splicing and/or insertion and naturally occurring allelic variants of SEQ ID NO: 6" would fall within the claims (page 3, lines 9-11, Office action dated 07/23/2004). The Examiner has also expressed concern regarding "non-productive receptors" (e.g., page 7, lines 23-24, Office action dated 3/28/2005).

Applicants note that the amended claims are directed to "contacting a human trkC receptor of SEQ ID NO: 6 expressed in neuronal cells with an antagonistic antibody capable of specifically binding to a full-length trkC receptor sequence comprising amino acid residues 32 to 839 of SEQ ID NO: 6, wherein said antibody binding inhibits the activity of said trkC receptor." Thus, the present claims are explicitly directed to inhibiting the activity of full-length trkC receptors. A trkC receptor without activity, such as a "non-productive receptor," or an inactive truncated or variant form, would not be inhibited, being already inactive. Accordingly concerns related to truncated or variant forms, or forms arising by alternate splicing, or non-productive receptors are believed to be moot in view of the present claims directed to inhibiting the activity of the full-length trkC receptor of SEQ ID NO: 6.

As discussed in previous responses (which are hereby incorporated by reference to avoid unnecessary duplication of argument), not only did the art recognize an association between neuronal sprouting and epilepsy, but moreover recognized that there was a relationship between trkC, NT-3, neuronal sprouting, and epilepsy at the time the application was filed. In particular, it was recognized that neuronal sprouting occurred in epilepsy, that there was a relationship between

NT-3 and neuronal sprouting (and thus a relationship between NT-3 and epilepsy), and that there was a relationship between trkC and epilepsy.

This recognition in the art at the time the application was filed, taken with the statement in the specification at page 68, lines 24-29 that "[t]his antagonist activity is believed to be useful in the treatment of pathological conditions associated with endogenous neurotrophin production, such as ... aberrant sprouting in epilepsy ..." would be understood by one of ordinary skill in the art to provide an explicit connection between a trkC receptor of SEQ ID NO: 6, aberrant neuronal sprouting, and a disease (epilepsy). Applicants note that the specification directly and explicitly discloses that the invention is useful in treating epilepsy. Moreover, it was recognized in the art at the time that aberrant sprouting was related to epilepsy, and that aberrant sprouting might be affected by neurotrophin levels and neurotrophin receptor activty. The disclosure in a patent specification is addressed to one of skill in the art; such a skilled person, with their knowledge of the art, reading the specification would have immediately recognized and appreciated the connection between inhibition of the activity of a trkC receptor of SEQ ID NO: 6 and the treatment of epilepsy. Accordingly, a nexus was established between a trkC of SEQ ID NO: 6 and aberrant sprouting in epilepsy, and would have been recognized as such by one of ordinary skill in the art.

In discussing the Bengzon reference, the Examiner suggests that "the data presented in the reference is not commensurate in scope with the claimed invention" as not being drawn "to protein but rather to mRNA levels (page 4, lines 11-13). However, applicants note that in a Declaration dated March 1, 2002, Jo-Anne Hongo stated that "Diseases where expression of Trk receptors correlate with the disease pathology are known in the art (see the Specification at page 4, lines 6-10, and page 68, lines 18-29). Based on the results of experiments summarized in this Declaration, it is my considered scientific opinion that molecules that antagonize neurotrophin or Trk activity (e.g., Trk-specific antibodies or Trk immunoadhesins) find use in the treatment of diseases characterized by neurotrophin or Trk receptor expression as determined by mRNA or protein assessment" (page 5, lines 8-13 (paragraph 10)). Thus, the Declaration directly points out that mRNA levels as well as protein levels are indicative of trk expression, and so directly addresses the Examiner's concerns about the Bengzon reference. Applicants submit that the Bengzon reference is indeed relevant and

may be relied upon to provide a nexus between trkC (SEQ ID NO: 6) protein antagonism, NT3, neuron sprouting and epilepsy.

The Examiner discusses the McNamara reference, noting that McNamara concludes that trkC, NGF and BDNF "may form part of the molecular machinery responsible for pathologic morphologic rearrangements" (page 6, lines 1-3 of the Office action dated 3/28/2005). However, the Examiner then goes on to suggest that the reference somehow "did not recognize a predictable nexus between trkC, NT3 and neuronal sprouting." This despite the clear conclusion of McNamara that trkC may be involved in pathologic morphologic rearrangements as acknowledged by the Examiner as quoted above; and despite the teachings of the other references discussed in the previous response. Moreover, Applicants again draw the Examiner's attention to the Declaration of Hongo, in which Hongo states that "Trk-specific antibodies ... find use in the treatment of diseases characterized by neurotrophin or Trk receptor expression as determined by mRNA or protein assessment" (Declaration of Hongo, page 5, lines 11-13). These remarks were directed to treatment of diseases such as those discussed in the "Specification at page 4, lines 6-10, and page 68, lines 18-29": e.g., aberrant neuronal sprouting (page 68, lines 28-29). Accordingly, Applicants believe that the Specification, references and the Declaration support the present claims.

The claims require that an antagonistic antibody of the invention be capable of specifically binding to a sequence within the amino acid residues 32 and 839 of SEQ ID NO: 6. The specification teaches such trkC receptors; as discussed above, such receptors would have been expected to be related to neuronal sprouting in epilepsy, and so such treatment would be expected to be useful and effective in such treatment. The specification provides guidance for such treatments, for example, at pages 69-71. Applicants submit that one of ordinary skill in the art, following the teachings of the specification, in view of the state of knowledge in the field, would have been enabled to make and use the invention without undue experimentation. Accordingly, Applicants respectfully submit that the rejections of claims 1, 4-7 and 23 under 35 U.S.C. § 112, first paragraph as allegedly not enabled are overcome.

The Rejections of Claims 1, 4-7, and 23 Under 35 U.S.C. §112, First Paragraph for Alleged Lack of Written Description

Claims 1, 4-7, and 23 stand rejected for alleged lack of written description in the specification. The rejection of the remaining claims is respectfully traversed.

The Examiner states that "Since the claims are drawn not only to full length SEQ ID NO: 6, but also to splice variants thereof ... the teachings of the specification do not provide an [sic] written description of the claimed invention..." (page 8, lines 16-20 of the Office action dated 3/28/2005). However, as amended, the claims are directed to methods using antibodies that specifically bind the full length trkC receptor of SEQ ID NO: 6 and inhibit its activity, and not to splice variants thereof.

Accordingly, Applicants respectfully submit that the specification provides an adequate written description of the claimed invention, and that the rejections of claims 1, 4-7, and 23 under 35 U.S.C. § 112, first paragraph for alleged lack of written description are overcome.

CONCLUSION

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** (**Attorney's Docket No. 39766-0033 CPC4C**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully Submitted,

Date: June 28, 2005

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